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09/494,585	01/31/2000	Richard A. Shimkets	15966-557(Cura-57)	3648

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EXAMINER
SAOUD, CHRISTINE J

ART UNIT	PAPER NUMBER
1647	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/494,585	Applicant(s) SHIMKETS et al.
	Examiner Christine Saoud	Art Unit 1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Oct 17, 2001*.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-10, 14, 19-21, 28, and 29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-10, 14, 19-21, 28, and 29* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [X] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [X] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4,8*

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

DETAILED ACTION

Response to Amendment

1. Claims 11-13, 15-18 and 22-27 have been canceled and claims 14, 19, and 21 have been amended as requested in the amendment of paper #11, filed 17 October 2001. Claims 1-10, 14, 19-21, and 28-29 are pending in the instant application.

2. Applicant's election without traverse of Group I in Paper No. 11 is acknowledged.

Specification

3. Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

4. The abstract of the disclosure is objected to because it uses the term "novel" and refers to speculative applications of the invention. Correction is required. See MPEP § 608.01(b).

Claim Objections

5. Claim 6 is objected to because of the following informalities: the word "least" is spelled incorrectly in line 2. Appropriate correction is required.

6. Claim 14 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 14 recites a "polypeptide at least 80% identical" and ultimately depends from claim 1 which recites "85% identical". Therefore, claim 14 is not further limiting.

7. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 recites "or an amino acid sequence comprising one or more conservative substitutions in the amino acid sequence of SEQ ID NO:2" and ultimately depends from claim 1 which recites "85% identical". Therefore, claim 5 is broader than claim 1, in that there is no upper limit on the number of substitutions, and can then encompass greater variability than "85%".

8. Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim. In the instant case, the oligonucleotide of claim 5 could be infringed without infringing the claim from which it depends, i.e. the nucleic acid which encodes the polypeptide. Therefore, the claim is improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 1-10, 19-21, 28-29 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of the nucleic acid, the encoded protein or the significance of either.

It is clear from the instant specification that the "FGF-CX" protein described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein, and the nucleic acid encoding it, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that

would support a conclusion that the "FGF-CX" protein of the instant application could be used in a method of diagnosing a tissue proliferation-associated disorder, "such as tumors, restenosis, psoriasis, diabetic and post-surgery complications, and rheumatoid arthritis" (see page 4, lines 26-28 of the specification), in a method of "treating or preventing or delaying a tissue proliferation-associated disorder" (page 5, lines 28-29 of the specification) by administration of a FGF-CX nucleic acid, polypeptide or antibody, wherein the disorder includes tumors, restenosis, psoriasis, Dupuytren's contracture, diabetic complications, Kaposi sarcoma, and rheumatoid arthritis (see page 6, lines 6-7 of the specification), in a method of treating or diagnosing glia-associated disorders, including "cerebral lesions, cerebral edema, senile dementia, Alzheimer's disease, diabetic neuropathies, etc." (see page 58, lines 2-4), stimulating fibroblasts, megakaryocytes, hematopoietic cells, immune system cells, vascular smooth muscle cells treating bone fractures and osteoporosis, diagnosis and treatment of cerebral tumors (see page 58, lines 11-16). Neither the specification nor the prior art demonstrates a correlation or nexus of the claimed nucleic acid molecule with any of the conditions or disorders contemplated by the instant specification, therefore, there is no evidence of record that would provide for a method of treating/diagnosing any of the listed conditions or disorders. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "FGF-CX" protein of the instant application is involved in regulating growth and/or differentiation of any *particular* cell population. The record fails to indicate any evidence of any of these biological activities, and it would appear that until some actual and specific significance can be attributed to the protein identified in the specification as FGF-CX, the gene encoding it, or the antibody that binds it, the instant invention is

incomplete. The instant specification refers to "FGF-CX - like activities and physiological functions" (page 11, line 15), but fails to describe what these activities or functions are. The specification asserts that the claimed nucleic acid will encode a protein which has activities similar to other FGF proteins based on amino acid sequence similarity, but it is not clear or predictive which activity of the FGF family will be possessed by the encoded protein based on structural similarity alone. The nucleic acid of the instant specification and the protein encoded thereby are compounds which are known to share some structural similarity to the FGF family of proteins which are known in the art to have biological significance in regulation of cell proliferation, differentiation, and function based on sequence similarity to members of the FGF-family. However, as indicated in Galzie et al. (Biochem. Cell Biol. 75: 669-685, 1997), the FGF family is complex and diverse (see abstract). Table 1 of Galzie et al. details the biological significance of the first 9 members of this protein family, wherein none of the associated functions are found in common with any other family member. In the absence of a knowledge of the biological significance of "FGF-CX", there is no immediately obvious patentable use for it or the receptor which binds it. The disclosed protein only shares approximately 70% amino acid sequence similarity/identity with the most closely related protein of the prior art. Based on this degree of sequence similarity, it is unlikely and unpredictable if any one biological activity of the prior art will be possessed by the claimed protein. Furthermore, the prior art of record demonstrates that the biological function of the protein family to which the disclosed protein is said to be a member is so diverse, that one could not predict which biological activity is possessed by the disclosed protein based on structural similarity alone, especially since all the members share structural

similarity, but not functional similarity. To employ the instant invention in any of the disclosed methods would clearly be using it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-10, 19-21, 28-29 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101.

13. Claims 1-10, 14, 19-21, 28-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 includes embodiments of polynucleotides encoding polypeptides having 85% sequence identity to SEQ ID NO:2, and claim 28 includes embodiments of polynucleotides which are derivatives, analogs, homologs and allelic variants of SEQ ID NO:1. The instant specification

fails to describe polynucleotides which meet these limitations of the claims. First, the instant specification teaches a single example of a polynucleotide which encodes a polypeptide (SEQ ID NO:1 and 2, respectively), and fails to teach any other nucleic acid sequences which encode a polypeptide having at least 85% identity, or derivatives, analogs, homologs and allelic variants of SEQ ID NO:1. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule (SEQ ID NO:1) which encodes a protein which has the amino acid sequence of SEQ ID NO:2. The subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed to nucleic acid molecules which encode polypeptide which have sequence identity or to derivatives, analogs, homologs, and variants of the disclosed nucleic acid of SEQ ID NO:1. First, the claims are not limited to any particular nucleic acid, in that the claims are also directed to variant forms thereof. The specification only describes a single nucleic acid and polypeptide and fails to teach or describe any other molecules which meet the structural limitations of the claims. The breadth of the claims is such that the claims encompass nucleic acids from other species, related nucleic acids and variant nucleic acids which have yet to be described. There is a lack of guidance or teaching regarding structure and function of the polypeptide because there is only a single example of a nucleic acids and polypeptide provided in the specification, because there is no

guidance found in the prior art for this nucleic acid or polypeptide, and because there is no known biological activity for the polypeptide.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the nucleic acid of SEQ ID NO:1 or a nucleic acid which encodes the polypeptide of SEQ ID NO:2. The specification does not provide a complete structure of those nucleic acid molecules which encode polypeptides which have at least 85% sequence identity to SEQ ID NO:2, or to derivatives, analogs, homologs, and variants of the disclosed nucleic acid of SEQ ID NO:1. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus because the specification teaches a single embodiment. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. Claims 14 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14 is directed to a method of producing a polypeptide. However, claim 14 ultimately depends from claim 1, which includes both encoding and complementary nucleic acid molecules. The instant specification fails to teach how to make a polypeptide using the complementary nucleic acid molecule which by definition does not encode the polypeptide, therefore, the claim is not enabled for such material.

Claim 29 is directed to a nucleic acid or fragment thereof, which has an activity. However, nucleic acids by themselves do not have activity, but rather they encode polypeptides which have activity. The instant specification fails to teach how to make a nucleic acid which possesses the activities listed in the claims, and therefore, the claim is not enabled for such molecules.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1, 3-4, 19-21, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 28 recite "FGF-CX", however, reference to this term is indefinite as it is not art recognized. Furthermore, as the claims are directed to nucleic acids encoding a sequence that is at least 85% identical to SEQ ID NO:2 or to fragments, derivatives, analogs, homologs, allelic variants, it is not clear that each and every structure that is at least 85% identical (etc.) will also encode "FGF-CX" as no characteristics of what is encompassed by this term are provided. Therefore, the metes and bounds of what is considered "FGF-CX" cannot be determined from the claim, and it is indefinite.

Claim 3 recites "said molecule encoding the human FGF-CX of SEQ ID NO:1". However, the sequence of SEQ ID NO:1 is the nucleic acid molecule, therefore, it is not clear what is intended by language directed to a nucleic acid encoding a nucleic acid sequence. It would appear that the claim should recite a nucleic acid molecule which has the sequence of SEQ ID NO:1, or the complement thereof (or something to that general effect).

Claim 4 recites "said molecule hybridizing under stringent conditions" and claim 28 recites hybridizes .... under stringent conditions", wherein such conditions are not recited in the claim. The metes and bounds of the recitation "hybridizing under stringent conditions" cannot be determined because, depending on the conditions which are used, many different molecules could be intended by the claims. There are multitude of hybridization conditions which are considered as "stringent" in the art, and without knowing which conditions are intended, the metes and bounds of the claim cannot be determined. The inclusion of those conditions which are intended by the recitation of "stringent", or reference to a specific definition in the specification (i.e. not optional conditions, or a range of conditions) would obviate this ground of rejection. Applicant

should note that any amendment to the claims may necessitate a new ground of rejection for another reason.

Claims 19-20 are indefinite for the recitation of "a therapeutically or prophylactically effective amount". The claim fails to indicate what the composition is to be therapeutically or prophylactically effective to do, therefore, such amounts cannot be determined from the claim and it is indefinite.

Claim 21 provides for the use of a therapeutic, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 21 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Applicant should note that if claim 21 is amended to be directed to a method of treatment by using the nucleic acid, it will be withdrawn as being directed to a non-elected invention.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 5 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Nauro et al. (U.S. Pat. No. 5,512,460).

Nauro et al. disclose and teach a nucleic acid molecule which meets the structural limitations of the instant claims in that it could be considered a "derivative" or "analog" or homolog" of SEQ ID NO:1, as well as encoding a protein which has glia activating activity (see SEQ ID NO:11 of Nauro et al.). The nucleic acid molecule of Nauro et al. does not encode "FGF-CX" as recited in claim 28, but in light of this term being indefinite for the reasons provided above, the claims are anticipated since all the structural limitations are met, absent evidence to the contrary. As claim 5 recites "or an amino acid sequence comprising one or more conservative substitutions in the amino acid sequence of SEQ ID NO:2", it would appear that this claim encompass any protein which has an unlimited number of amino acid substitutions, therefore, the nucleic acid molecule of Nauro et al. meet these structural limitations as well.

19. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Nauro et al.

Nauro et al. disclose a nucleic acid molecule (SEQ ID NO:11) which shares sequence similarity with the claimed nucleic acid molecule of the instant specification (SEQ ID NO:1), including several stretches of at least 6 contiguous nucleotides. Claim 6 is directed to an oligonucleotide of less than 100 nucleotides and comprising 6 contiguous nucleotides of SEQ ID NO:1. Nauro et al. teach isolation of 67 bp fragments of the nucleic acid molecule encoding glia

activating factor (column 25, Example 5), therefore, Nauro et al. disclose oligonucleotides which meet the limitations of the claim and anticipates the instant claim, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 19, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud